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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,768	07/25/2003	Jean-Paul Giacobino	4-30353B/D1	4303

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 430/2
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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,768	GIACOBINO ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7-11 and 19-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *10 and 19-22* is/are rejected.

7)☐ Claim(s) *2,7-9 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/423,410.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/04/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 04/21/04 has been acknowledged.
Claims 3-6, 12-18 are canceled.
Claims 19-22 are newly filed.
Claims 1-2, 7-11 and 19-22 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised **37 CFR §1.121**. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.

Claim Objections

Claims 2, 7-11 are objected to because of the following informalities:

Claim 2 recites claim limitation "DNA fragment according to Claim 1". Changing "DNA fragment according to Claim 1" to "The DNA fragment according to claim 1" has been suggested.

Claims 7 and 8 recites claim limitation "a DNA sequence according to claim 1". Changing "a DNA sequence according to claim 1" to "the DNA sequence according to claim 1" has been suggested.

Claim 9-10 are objected to as being dependent upon an objected base claim, but would be allowable if rewritten independent form including all of the limitation of the base claim and any intervening claims.

Claim 10 recites claim limitation "vector of Claim 9". Changing "vector of Claim 9" to "vector of claim 9" has been suggested.

Claim 11 recites claim limitation "A recombinant DNA molecule deposited with the ATCC as ATCC NO 97999". To clearly define the claimed subject matter following language has been suggested -- A recombinant DNA molecule of SEQ ID NO: 3 deposited with the ATCC as ATCC NO 97999 --

Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities: The specification should be amended to reflect the change in the address of the ATCC, whose new address is 10801 University Boulevard Manassas, VA 20110-2209, USA (see specification page 4).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 21 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim is drawn to an isolated DNA fragment having a sequence homologous to the DNA nucleotide sequence of a DNA fragment encoding $UCP3_L$ SEQ ID NO:4. The scope of invention as claimed encompasses any and all variants of a DNA fragment encoding the amino acid sequences of SEQ ID NO:4, wherein in the variant is derived form any natural and/or non-natural source. At best the specification as filed discloses nucleic acid sequences of SEQ ID NO:3 which encodes the amino acid sequences of SEQ ID NO:4 ($UCP3_L$). The specification as filed fails to disclose any variant of nucleic acid encoding the amino acid sequences of SEQ ID NO:4 that has the functional property of $UCP3_L$ polypeptide explicitly or implicitly as putatively claimed by the instant invention.

Applicant is referred to the guidelines for ***Writt n D scription Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In instant case the specification only discloses nucleic acid sequences of SEQ ID NO:3 which encodes the amino acid sequences of SEQ ID NO:4 ($UCP3_L$).

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the nucleic acid variants (as claimed) has been defined only by a statement of function that broadly encompasses $UCP3_L$-like activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics.

In addition, it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, since the relationship between the

sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. Furthermore, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA fragment comprising the nucleotide sequence of SEQ ID NO:3, which encodes the amino acid sequences of SEQ ID NO:4 , does not reasonably provide enablement for any sequence homologous to the DNA nucleotide encoding the amino acid sequences of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of Invention:

The instant invention relates to nucleic acid sequences encoding an uncoupling protein ($UCP3_L$).

Breadth of Claims and Guidance Provided in the Specification

The instant claim is drawn to an isolated DNA fragment having a sequence homologous to the DNA nucleotide sequence of a DNA fragment encoding $UCP3_L$ SEQ ID NO:4. The scope of invention as claimed encompasses any and all variants of a DNA fragment encoding the amino acid sequences of SEQ ID NO:4, wherein in the variant is derived form any natural and/or non-natural source. At best the specification as filed discloses nucleic acid sequences of SEQ ID NO:3 which encodes the amino

acid sequences of SEQ ID NO:4 ($UCP3_L$). The specification as filed fails to disclose any variant of nucleic acid encoding the amino acid sequences of SEQ ID NO:4 that has the functional property of $UCP3_L$ polypeptide explicitly or implicitly as putatively claimed by the instant invention.

State of Art and Predictability

The state of the art regarding uncoupling protein UCP3 teaches that the UCP3 is expressed in large amount in human skeletal muscle and is involved in the regulation of thermo-genesis in skeletal muscles. Two UCP3 mRNAs are present in vivo, the full length transcript UCP3L and a shorter form UCP3S, which arises from a cleavage and polyadenylation signal located in the last intron that prematurely terminates about half of the transcripts. UCP3L encodes a 312 amino acid protein while UCP3S encodes a 275 aa protein lacking the sixth transmembrane spanning domain. UCPs are imported into mitochondria and inserted into the inner membrane by an import machinery specialized for membrane proteins. Mitochondrial targeting information for import by this pathway is present in the mature protein, rather than in an N-terminal signal sequence that is removed after import. The sixth membrane spanning domain of the ADP/ATP carrier, a protein closely related to UCP3, is required for its membrane potential dependent insertion into the mitochondrial inner membrane. As this domain is missing from UCP3S, there may be significant differences in the mitochondrial insertion of the two UCP3 isoforms (Renold et al FEBS Lett. 465(2-3):135-40, 2000). Therefore it would be unpredictable that a homologous polypeptide containing any addition, substitution, or deletion over the entire length of nucleic acid sequences encoding the SEQ ID NO:4 would have $UCP3_L$-like activity.

In addition it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The homologous sequences (variants) as claimed are mere hypothetical

polypeptides because no biological function has been established. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore, Applicant has not presented enablement commensurate in scope with the claims.

Considering the unpredictability in the art and the limited amount of guidance provided in the instant application it is unclear how one skill in the art would exercise the invention as claimed without further undue amount of experimentation. In instant case screening of any and all natural and non-natural variants of $UCP3_L$ polypeptide, wherein unknown numbers of amino acid sequences are added substituted and /or deleted when compared to the amino acid sequences of SEQ ID NO: 4 is not considered routine. Making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein unknown amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed $UCP3_L$ activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as

claimed since the applicant has not presented enablement commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 contains the trademark/trade name **pBluescript SK⁻**. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a plasmid construct and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention ther of by the applicant for patent, or on an international application

by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 19-22 are rejected under 35 U.S.C. 102(e) as being antibcipated by Beeley et al (US 6187560 2001, 102(e) date 06/30/1997; foreign priority date 03/05/1997).

The instant claims are drawn to a an isolated DNA fragment encoding the amino acid sequences of SEQ ID NO: 4 and a host cell comprising the DNA fragment.

Regarding claims 19 and 21 Beeley teaches an amino acid sequence (SEQ ID NO:2) which matches 100% to the amino acid sequences of SEQ ID NO:4 of instant application (see attached PTO sequence search report conducted 05/19/04). The cited art further teaches nucleic acid sequences corresponding to the amino acid sequences which matches the amino acid sequences of SEQ ID NO:4 of instant application (see Beeley fig-1). Regarding claim 20 the cited art teaches that the polynucleotide encoding HNFCW60 (SEQ ID NO:2) are obtained using standard cloning and screening, from a cDNA library derived from cells of human brain frontal cortex, rhabdomyosarcoma, fetal heart, and skeletal muscle (Col.4 lines 57-61). Regarding claim 22 the cited art teaches making of recombinant protein usijg genetically engineered host cells comprising the HNFCW60 polypeptide (col. 6 lines 16-45). Thus the cited art clearly anticipate the invention as claimed.

Conclusion

Claim 1 is allowable.

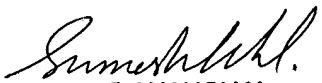
Claims 10, 19-22 are rejected.

Claims 2, 7-9 and 11 are objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sumesh Kaushal
Examiner GAU 1636



SUMESH KAUSHAL
PATENT EXAMINER